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ORIGINAL ARTICLE

Peripheral nerve involvement in Behçet's disease; an electrophysiological study



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Abstract Behçet's disease (BD) is a chronic inflammatory disease which is best described as a multisystem vasculitis. Central nervous system involvement is common in BD, but peripheral nerve involvement is uncommon.

Aim of the work: To determine peripheral nerve involvement; both clinically and electrophysiologically in Behçet patients and to study its relation to disease duration and activity scores.

Patients and methods: This study was carried out on 18 patients suffering from BD. Disease activity was assessed by Behçet Disease Current Activity Form (BDCAF). Peripheral neuropathy was assessed by the reduced version of the Total Neuropathy Score. Electrophysiological studies including nerve conduction studies and F waves of peripheral nerves were performed on all patients.

Results: There was a significant difference in the percentage of sensory and motor nerve affection ($p < 0.05$) in BD patients. Sural nerve latencies and conduction velocities were abnormal in 50% of patients on the right and in 44.4% of patients on the left side. Sural nerve latencies were significantly correlated with disease duration ($p < 0.05$ for right side and $p < 0.01$ for left side). Correlations between F wave frequencies and disease duration were significant for right and left peroneal nerves ($p < 0.01$ and $p < 0.05$ respectively) and highly significant for right and left median nerves ($p < 0.001$).

Conclusion: Peripheral nerve involvement is present in BD. The longer the disease duration; the more is the affection of the peripheral nerves. Full neurological assessment and electrophysiological studies are necessary in the follow up of Behçet patients.

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1. Introduction

Behçet's disease (BD) is a chronic inflammatory disease which is best described as a multi-system vasculitis, and is associated with protean manifestations including mucocutaneous lesions,

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ocular disease, neurologic disease, vascular disease and arthritis [1]. The first description of Behçet's disease was probably by Hippocrates in the fifth century BC [2] and the first modern account was presented in 1937 by the Turkish dermatologist Hulusi Behçet, who reported a patient with recurrent oral and genital aphthae and uveitis [3].

The classification of this condition depends on the presence of clinical features as defined by the International Study Group (ISG) on Behçet's Disease [4]. Aphthous oral ulcers are usually the first and most persistent clinical feature of BD. Lesions occur in crops and are discrete, painful, round or oval red-rimmed lesions that affect mainly the non keratinized mucosa of the cheeks, the border of the tongue, the soft palate, and the pharynx. Genital ulcers occur as single or multiple lesions of the vulva, vagina, scrotum or penile shaft and are usually painful and may result in scarring [5].

Ophthalmologic manifestations of Behçet's disease include anterior/posterior uveitis, conjunctivitis, corneal ulceration, papillitis and arteritis [6]. Uveitis is the most common type of eye involvement in Behçet's disease. It is usually chronic, bilateral and episodic often involving the entire uveal tract. Hypopyon is associated with a poor prognosis owing to its association with retinal vasculitis [7].

Neuro-BD is more frequent in young males and it never represents a presenting feature of the disease. The most frequent time of onset of neurological involvement seems to be within the first 10 years of disease [8]. In a study on 53 Egyptian patients with BD, 39.62% had neuro-BD and the disease activity score was significantly higher in those with neuro-Behçets compared to those without [9]. In another study, neurological manifestations were present in 20.41% BD Egyptian patients [10]. In neuro-BD (NBD), the CNS can be involved in two ways: first, and most commonly, through the development of an immune-mediated meningoencephalitis, which predominantly involves the brainstem, but can also involve the basal ganglia, thalamus, cortex and white matter, spinal cord, or cranial nerves; and second, as a consequence of thrombosis within the dural venous sinuses [11]. Brainstem involvement bears a poorer prognosis because it is linked with a progressive evolution [12]. Neuro-Behçet's disease (NBD) presents cognitive and behavioral symptoms [13]. The headache in NBD may be subacute, moderate to severe headache with unilateral localization and throbbing quality accompanied by nausea, vomiting, and aggravation upon awakening [14]. Ruptured aneurysms, peripheral neuropathy, optic neuritis, and vestibular involvement can occur [15]. Behçet patients may have subclinical peripheral nerve involvement. The frequency of neuropathy was higher in the patients with BD when compared with the control subjects [16].

Although peripheral neuropathy is uncommon [17], conventional electrophysiologic nerve conduction studies including F responses are recommended in a routine examination to diagnose early neuropathy in Behçet patients.

The aim of this study was to evaluate the peripheral nervous system of BD patients electrophysiologically and to find out if electrophysiological abnormalities are correlated with disease duration and activity scores or not.

2. Patients and methods

2.1. Selection of patients

Eighteen patients diagnosed as BD were enrolled into this study. They were selected from the inpatient departments and outpatient clinics of Rheumatology and Rehabilitation and of Dermatology, Venereology and Andrology Departments, Faculty of Medicine, Zagazig University Hospitals. All patients fulfilled the criteria of the International Study Group (ISG) for BD [4]. Patients with diabetes mellitus, hereditary neuropathies or those with symptoms of motor or sensory impairment prior to the onset of BD were excluded from the study.

The study was approved by the Local Ethics Committee of the university. An informed consent was obtained from each patient.

2.2. Clinical evaluation of patients

Active and inactive BD was determined by using BD current Activity score form (BDCAF) [18]. It depends on the presence of symptoms over the last 4 weeks prior to assessment.

We used the reduced version of the Total Neuropathy Score (TNS) for neurological assessment of the patients [19]. It comprises five categories, each graded from 0 to 4, for a total score range of 0–20 points. Categories included the extent and severity of sensory and motor symptom reports, assessment of deep tendon reflexes, muscle strength testing, vibration sensibility (128-Hz tuning fork), and pin prick sensibility.

2.3. Electrophysiological studies

Electrophysiological studies of the upper and lower limbs were performed at room temperature, using Viking Quest Nicolet electromyography equipment. Motor and sensory conduction studies of the median and ulnar nerves and median nerve F-wave latencies and frequencies were assessed bilaterally. Motor conduction studies of tibial and peroneal nerves, sensory conduction studies of sural nerve and peroneal nerve F-wave were also assessed bilaterally. Superficial disk electrodes were used for motor and sensory conduction studies. Electrophysiological studies and normal reference values were evaluated according to the description of Preston and Shapiro [20].

For motor conduction studies, the recording electrodes were placed over the abductor pollicis brevis muscle for the median nerve, the adductor digiti minimi muscle for the ulnar nerve, the extensor digitorum brevis muscle for the peroneal nerve and the abductor hallucis brevis muscle for the tibial nerve. The active recording electrode was placed on the belly of the examined muscle and the reference electrode was placed on the tendon insertion.

Sensory conduction studies were performed using the antidromic method. Digit2-wrist segment was used for median sensory nerve conduction studies. Digit5-wrist segment was used for ulnar sensory nerve conduction studies. Sensory conduction studies of the sural nerve were performed by placing the recording electrode posterior to the lateral malleolus and the

reference electrode 3–4 cm distally and stimulating the sural nerve at the posterolateral aspect of the leg 14 cm proximal to the active electrode.

F-wave study was performed for the median and peroneal nerves by recording from the same muscles used for motor studies. An active stimulating electrode was placed proximally and at least 10 successive supra-maximal stimulations were given. Minimum F-wave latencies and frequencies were recorded.

Motor nerve conduction velocities were considered abnormal if below 49 m/s for the upper limb or below 44 m/s for the lower limb. Distal motor latencies were considered prolonged if higher than 4.4 ms for the median nerve, 3.3 ms for the ulnar nerve, 6.5 ms for the peroneal nerve and 5.8 ms for the tibial nerve.

Sensory nerve conduction velocity of the median and ulnar nerves were considered abnormal if below 50 m/s. Peak latencies were considered abnormal if higher than 3.5 and 3.1 ms for the median and ulnar nerves, respectively. Sensory nerve conduction velocity and peak latency of the sural nerve were considered abnormal if below 40 m/s and above 4.4 ms respectively.

F-wave latencies were considered abnormal if higher than 31, 56 ms for the median and peroneal nerves, respectively. F-wave frequencies less than 50 % were considered abnormal in all the studied nerves.

Statistical analysis: Data were analyzed using SPSS software package version 18.0 (SPSS, Chicago, IL, USA). Quantitative data were expressed using range, mean and standard deviation, while qualitative data were expressed in frequency and percent. Quantitative data were analyzed using Mann–Whitney test & Spearman coefficient. The *p* value was assumed to be significant at 0.05 or less.

3. Results

3.1. Demographic data

This study included 18 patients suffering from BD. They were 11 males and 7 females. Their ages ranged from 19 to 43 years and their disease durations ranged from 2 to 17 years.

3.2. Clinical and electrophysiological characteristics

Patients involved in this study had disease activities ranging from 0 to 13, their scores in the TNS ranged from 0 to 2. By clinical examination, 2 patients (11.1%) had sensory symptoms in the form of tingling and numbness, 4 patients (22.2%) had reduced sensation up to the wrist and/or ankle and 2 patients had motor manifestations in the form of mild distal weakness. None of our patients had lost reflexes. The demographic and clinical characteristics in BD patients are shown in [Table 1](#). [Table 2](#) presents the nerve conduction study findings in BD patients

3.3. Abnormal electrophysiological findings in BD patients

[Table 3](#) demonstrates the frequencies of electrophysiological abnormalities in BD patients. The most prominent electrophysiological abnormality in BD patients was the abnormal sural nerve latency and conduction velocity. Sensory nerve

Table 1 Demographic and clinical characteristics in Behçet's disease patients.

Characteristic	Range	Mean \pm SD
Age (years)	19–43	30.67 \pm 9.91
Disease duration (years)	2–17	6.83 \pm 4.27
BDCAF score	0–13	6.61 \pm 3.45
TNS	0–2	1.50 \pm 2.38
Clinical items of BDCAF	No. (%)	
Headache	6 (33.3)	
Oral ulceration	9 (50)	
Genital ulceration	4 (22.2)	
Erythema	2 (11.1)	
Skin pustules	4 (22.2)	
Arthralgia	10 (55.6)	
Arthritis	2 (11.1)	
Nausea/vomiting/abdominal pain	8 (44.4)	
Diarrhea + altered/frank blood per rectum	3 (16.7)	
Eye involvement	7 (38.9)	
CNS involvement	4 (22.2)	
Major vessel involvement	2 (11.1)	

TNS: Total Neuropathy Score, BDCAF: Behçet Disease Current Activity Form.

Table 2 Nerve conduction study findings in Behçet's disease patients.

		Range	Mean \pm SD
Ulnar n. sensory latency	(right)	2.5–3.6	2.29 \pm 0.34
	(left)	2.6–3.7	2.97 \pm 0.33
Sural n. latency	(right)	3.8–5.2	4.48 \pm 0.56
	(left)	3.7–5.3	4.51 \pm 0.58
Median n. F wave frequency	(right)	18–85%	57 \pm 0.21
	(left)	0–74%	53 \pm 0.21
Peroneal n. F wave frequency	(right)	0–70%	32 \pm 0.28
	(left)	0–72%	36 \pm 0.29

conduction studies of ulnar, median and sural nerves (16.6%, 22.2%, 50% respectively) were more affected than motor nerve conduction studies of the ulnar, median, tibial and peroneal nerves (11.1%, 5.6%, 16.7%, 11.1% respectively) and the difference was significant ($t = 4.3$, $p < 0.05$).

3.4. Correlations between Behçet's disease duration and disease activity and the most frequent electrophysiological abnormalities

Sural nerve latencies were significantly correlated with the disease duration ($p < 0.05$) ([Fig. 1](#)), and the peroneal F wave frequencies showed statistically significant negative correlations with the disease duration ($p < 0.05$) ([Fig. 2](#)).

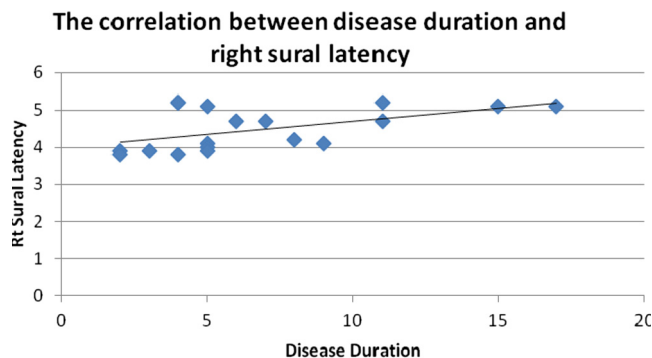
Regarding disease activity, there were positive correlations between sural nerve latencies and disease activity scores and negative correlations between the peroneal F wave frequencies & disease activity scores, but these correlations did not reach statistically significant levels ($p > 0.05$).

4. Discussion

The central nervous system is frequently involved in BD, but peripheral neuropathy, which is seen frequently in other

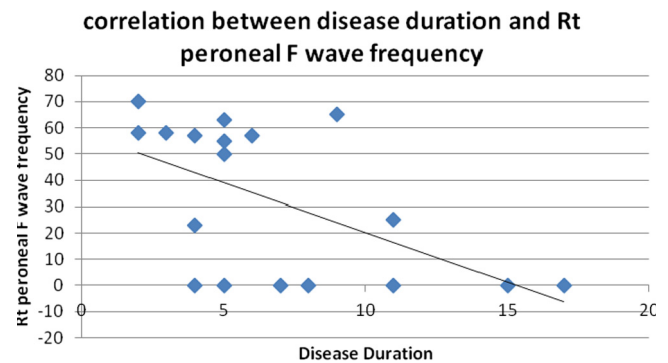
Table 3 Frequencies of electrophysiological abnormalities in Behçet's disease patients.

The studied nerve			Abnormality N (%)
<i>Latency and conduction velocity</i>			
Ulnar nerve	Motor	(right)	1 (5.6)
		(left)	1 (5.6)
	Sensory	(right)	3 (16.6)
		(left)	4 (22.2)
Median nerve	Motor	(right)	1 (5.6)
		(left)	0 (0)
	Sensory	(right)	4 (22.2)
		(left)	4 (22.2)
Tibial nerve	Motor	(right)	2 (11.1)
		(left)	1 (5.6)
Peroneal nerve	Motor	(right)	1 (5.6)
		(left)	1 (5.6)
Sural nerve		(right)	9 (50)
		(left)	8 (44.4)
<i>F wave frequency</i>			
Median nerve		(right)	6 (33.3)
		(left)	5 (27.8)
Peroneal nerve		(right)	9 (50)
		(left)	7 (41.2)

**Figure 1** Correlation between right sural nerve latencies and disease duration in Behçet's disease patients.

vasculitides, is very uncommon in BD [21]. However, other case reports and studies have revealed the involvement of the peripheral nervous system. In 2005, Ghorbel et al. reported a 47 year old male with 6 year duration BD with paresthesia and weakness of the upper and lower limbs, diarrhea and erectile dysfunction & EMG evidence of axonal sensorimotor neuropathy and nerve biopsy showing axonal neuropathy [22]. In 2007, Akubulat et al. performed an electrophysiological study on Behçet patients and stated that they may have subclinical peripheral nerve involvement [16]. Eun and colleagues reported a 39-yr-old female patient presenting with recurrent tibial neuropathy and concluded that BD should be considered in patients with idiopathic recurrent mononeuropathy [23]. In this study, we assessed the peripheral nervous system in BD patients both clinically and electrophysiologically.

In our study, patients presenting with sensory manifestations (22.2%) were more than those presenting with motor manifestations (11.1%). Sensory nerve conduction studies of

**Figure 2** Correlation between right peroneal F wave frequencies and disease duration in Behçet's disease patients.

ulnar, median and sural nerves (16.6%, 22.2%, 50% respectively) were more affected than motor nerve conduction studies of the ulnar, median, tibial and peroneal nerves (11.1%, 5.6%, 16.7%, 11.1% respectively) and the difference was significant ($t = 4.3$, $p < 0.05$). These findings were similar to those of Akubulat et al., who also stated that sensory nerves were affected more prominently than motor nerves [16]. Birol et al., hypothesized that the nerve dysfunction or peripheral neuropathy of BD is a distal polyneuropathy that predominantly involves the lower extremities [24]. This hypothesis goes with our study in which the sural nerve was the most frequently affected nerve in our patients (50%).

F waves were affected in (50%) of our patients in the form of infrequent F waves, these findings were similar to those of Budak et al., who also studied conventional nerve conduction studies in Behçet patients and found that the F wave persistence was decreased [25].

In our study right and left sural nerve latencies correlated significantly with the disease duration ($r = 0.529$, $p < 0.05$ and $r = 0.598$, $p < 0.01$). No significant correlation was found between right & left sural nerve latencies and disease activity scores ($r = 0.147$, $p > 0.05$ and $r = 0.286$, $p > 0.05$ respectively). Correlations between F wave frequencies and disease duration were significant for Rt & Lt peroneal ($r = -0.56$, $p < 0.01$ and $r = -0.518$, $p < 0.05$ respectively). Correlations between F wave frequencies and disease activity were non-significant ($p > 0.05$) for Rt and left peroneal and median nerves. These findings were similar to those of Akubulat et al., who found no significant difference between the clinical parameters of the patients with and without electrophysiologically detected neuropathy, except disease duration [16].

From this work we conclude that peripheral nerve involvement is present in BD. Peripheral nerve affection in BD is predominantly sensory affecting the lower limbs. The longer the disease duration the more the peripheral nerves are affected. Full neurological assessment and electrophysiological studies including nerve conduction and F waves are necessary in the follow up of Behçet patients.

Conflict of interest

The authors have no conflict of interest to declare.

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